

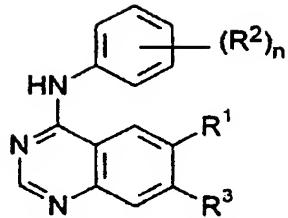
Amendments to the Claims:

JC17 Rec'd PCT/PTO 28 JUN 2005

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Original) A preventive and/or therapeutic agent for psychosis containing an inhibitor of epidermal growth factor receptor as the active ingredient.
2. (Original) The preventive and/or therapeutic agent according to claim 1, wherein the inhibition is a competitive inhibition on binding between epidermal growth factor receptor and epidermal growth factor.
3. (Original) A preventive and/or therapeutic agent for schizophrenia containing an inhibitor of epidermal growth factor receptor as the active ingredient.
4. (Original) The preventive and/or therapeutic agent according to claim 3, wherein the inhibition is a competitive inhibition on binding between epidermal growth factor receptor and epidermal growth factor.
5. (Original) A preventive and/or therapeutic agent for cognitive abnormalities containing an inhibitor of epidermal growth factor receptor as the active ingredient.
6. (Original) The preventive and/or therapeutic agent according to claim 5, wherein the inhibition is a competitive inhibition on binding between epidermal growth factor receptor and epidermal growth factor.
7. (Currently Amended) The preventive and/or therapeutic agent according to claim 1 or claim 3 or claim 5 containing a quinazoline derivative having inhibitory activity to epidermal growth factor receptor represented by the chemical formula I, a stereoisomer thereof, a pharmaceutically-acceptable salt thereof, its hydrate or its solvate as the effective ingredient, ingredient.

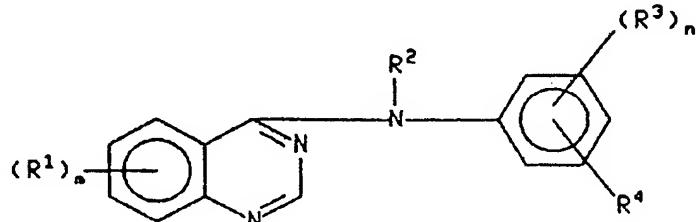


<Formula I>

wherein n is 1, 2 or 3 and R² is each independently halogen, trifluoromethyl, or (1-4C) alkoxy; R³ is (1-4C) alkoxy; and R¹ is di-[(1-4C)alkyl]amino-(2-4C)alkoxy, pyrrolidin-1-yl-(2-4C)alkoxy, piperidino-(2-4C)alkoxy, morpholino-(2-4C)alkoxy, piperazin-1-yl-(2-4C)alkoxy, 4-(1-4C)alkylpiperazin-1-yl-(2-4C)alkoxy, imidazol-1-yl-(2-4C)alkoxy, di-[(1-4C)alkoxy-(2-4C)alkyl]amino-(2-4C)alkoxy, thiamorpholino-(2-4C)alkoxy, 1-oxothiamorpholino-(2-4C)alkoxy or 1,1-dioxothiamorpholino-(2-4C)alkoxy, and,

wherein any of the above-mentioned R¹ substituents comprising a CH₂ (methylene) group which is not attached to N or O atom optionally bears a hydroxy substituent on said CH₂ group.

8. (Currently Amended) The preventive and/or therapeutic agent according to claim 1 or claim 3 or claim 5 containing a quinazoline derivative represented by the chemical formula II, a stereoisomer thereof, a pharmaceutically-acceptable salt thereof, its hydrate or its solvate as the effective ingredient,

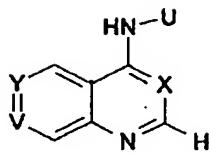


<Formula II>

wherein; m is 1, 2, or 3; R¹ is each independently selected from the group consisting of hydrogen, halo, hydroxy, amino, hydroxyamino, carboxy, (C₁-C₄)alkoxycarbonyl, nitro, guanidino, ureido, carbamoyl, cyano, trifluoromethyl, (R⁶)₂N-carbonyl, and phenyl-W-alkyl (wherein W is selected from the group consisting of a single bond, O, S and NH); or R¹ is each independently selected from the group consisting of cyano-(C₁-C₄)-alkyl and R⁹ (wherein R⁹ is selected from the group consisting of R⁵, R⁵O, (R⁶)₂N, R⁷C(=O), R⁵ONH, A

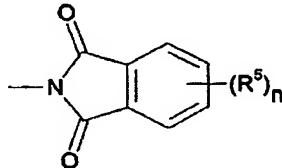
and R⁵Y; R⁵ is (C₁-C₄)alkyl; R⁶ is hydrogen or R⁵ wherein the R⁵'s are the same or different; R⁷ is R⁵, R⁵O or (R⁶)₂N ;A is selected from the group consisting of piperidino-, morpholino, pyrrolidino and 4-R⁶-piperazin-1-yl, imidazol-1-yl, 4-pyridon-1-yl, carboxy-(C₁-C₄)-alkyl, phenoxy, phenyl, phenylsulfanyl, (C₂-C₄)-alkenyl, (R⁶)₂N-carbonyl-(C₁-C₄)-alkyl; and Y is selected from the group consisting of S, SO, SO₂; the alkyl moieties in R⁵, R⁵O and (R⁶)₂N are halo or R⁹ (wherein R⁹ is defined as above) and wherein the resulting groups are optionally substituted with halo or R⁹, with the proviso that a nitrogen, oxygen or sulfur atom and another heteroatom can not be attached to the same carbon atom, and with the further proviso that no more than three "R⁹" units may comprise R¹; or each R¹ is each independently selected from the group consisting of R⁵-sulfonylamono, phthalimido-(C₁-C₄)-alkylsulfonylamino, benzamido, benzenesulfonylamino, 3-phenylureido, 2-oxopyrrolidin-1-yl, 2,5-dioxopyrrolidin-1-yl, and R¹⁰-(C₂-C₄)-alkanoylamino (wherein R¹⁰ is selected from halo, R⁶O, (C₂-C₄)-alkanoyloxy, R⁷C(=O), and (R⁵)₂N; and wherein said benzamido or benzenesulfonylamino or phenyl or phenoxy or anilino or phenylsulfanyl substituent in R¹ may optionally bear one or two halogens, (C₁-C₄) alkyl, cyano, methansulfonyl or (C₁-C₄)-alkoxy substituents); or any two R¹'s taken together with the carbons to which they are attached may comprise a 5-8 membered ring comprising at least one or two heteroatoms selected from oxygen, sulfur or nitrogen; and wherein the alkyl groups and alkyl portions of the alkoxy or alkylamino groups may be straight chained or if comprised of at least three carbons may be branched or cyclic; R² is selected from hydrogen and optionally substituted(C₁-C₆)-alkyl; n is 1 or 2 and each R³ is independently selected from hydrogen, optionally substituted (C₁-C₆)-alkyl, optionally substituted amino, halo, hydroxy, optionally substituted hydroxy; R⁴ is azido or R¹¹-ethynyl (wherein R¹¹ is selected from hydrogen, optionally substituted(C₁-C₆)alkyl, wherein the substituents are selected from the group consisting of hydrogen, amino, hydroxy, R⁵O, R⁵NH and (R⁵)₂N.

9. (Currently Amended) The preventive and/or therapeutic agent according to claim 1-~~or claim 3 or claim 5~~ containing a quinazoline derivative having inhibitory activity to epidermal growth factor receptor represented by the chemical formula III, a stereoisomer thereof, a pharmaceutically-acceptable salt thereof, its hydrate or its solvate as the effective ingredient,



<Formula III>

wherein X is N or CH; Y is CR¹ and V is N; or Y is N and V is CR¹; or Y is CR¹ and V is CR²; or Y is CR² and V is CR¹; R¹ represents a group CH₃SO₂CH₂CH₂NHCH₂-Ar-, (wherein Ar is selected from the group consisting of phenyl, furan, thiophene, pyrrole and thiazole, each of which may optionally be substituted by one or two halo, C₁₋₄ alkyl or C₁₋₄ alkoxy groups); R² is selected from the group consisting of hydrogen, halo, hydroxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ alkylamino and di[C₁₋₄ alkyl]amino; U represents a phenyl, pyridyl, 3H-imidazolyl, indolyl, isoindolyl, indolinyl, isoindolinyl, 1H-indazolyl, 2,3-dihydro-1H-indazolyl, 1H-benzimidazolyl, 2,3-dihydro-1H-benzimidazolyl and 1H-benzotriazolyl group, substituted by an R³ group and optionally substituted by at least one R⁴ group selected independently ; R³ is selected from a group consisting of benzyl, halo-, dihalo- and trihalobenzyl, benzoyl, pyridylmethyl, pyridylmethoxy, phenoxy, benzyloxy, halo-, dihalo- and trihalobenzyloxy and benzenesulphonyl; or R³ represents trihalomethylbenzyl or trihalomethylbenzyloxy; or R³ represents a group of formula IV



<Formula IV>

wherein each R⁵ is independently selected from the group consisting of halogen, C₁₋₄ alkyl and C₁₋₄ alkoxy; and n is 0 to 3; each R⁴ is independently hydroxy, halogen, C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, C₁₋₄ alkoxy, amino, C₁₋₄ alkylamino, di[C₁₋₄ alkyl]amino, C₁₋₄ alkylthio, C₁₋₄ alkylsulphanyl, C₁₋₄ alkylsulphonyl, C₁₋₄ alkylcarbonyl, carboxy, carbamoyl, C₁₋₄ alkoxy carbonyl, C₁₋₄ alkanoylamino, N-(C₁₋₄ alkyl)carbamoyl, N,N-di(C₁₋₄ alkyl)carbamoyl, cyano, nitro and trifluoromethyl; with the proviso that the following compounds and their hydrochloride salts are excluded:

(1-Benzyl-1H-indazol-5-yl)-(6-(5-((2-methanesulphonyl-ethylamino)-methyl)-furan-2-yl)-pyrido[3,4-d]pyrimidin-4-yl-amine;

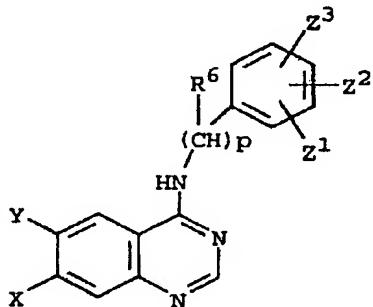
(4-Benzyl-1H-indazol-5-yl)-(6-(5-((2-methanesulphonyl-ethylamino)-methyl)-furan-2-yl)-pyrido[3,4-d]pyrimidin-4-yl-amine;

(1-Benzyl-1H-indazol-5-yl)-(6-(5-((2-methanesulphonyl-ethylamino)-methyl)-furan-2-yl)-quinazolin-4-yl-amine;

(1-Benzyl-1H-indazol-5-yl)-(7-(5-((2-methanesulphonyl-ethylamino)-methyl)-furan-2-yl)-quinazolin-4-yl-amine;

(1-Benzyl-1H-indazol-5-yl)-(6-(5-((2-methanesulphonyl-ethylamino)-methyl)-1-methyl-pyrrol-2-yl)-quinazolin-4-yl-amine).

10. (Currently Amended) The preventive and/or therapeutic agent according to claim 1-~~or claim 3- or claim 5~~ containing a quinazoline derivative having inhibitory activity to epidermal growth factor receptor represented by the chemical formula V, a stereoisomer thereof, a pharmaceutically-acceptable salt thereof, its hydrate or its solvate as the effective ingredient,



<Formula V>

wherein

X is -D-E-F and Y is -SR⁴, -OR⁴, -NHR³, or hydrogen, or X is -SR⁴, -OR⁴, -NHR³, or hydrogen, and Y is -D-E-F ;

D is NR²-, -O-, -CHR²-, -NR²-NH-, -NR²-O-, -CHR²-O-, -CHR²-CH₂-, -CHR²-CH₂-, NH-CHR²-, -O=CHR²-, -S-CHR²-, or D does not exist;

E is -CO-, -SO₂-, -PO(OR²)-, or -SO-;

F is -CR¹=CHR⁵-, -C≡C-R⁵-, -CR¹=C=CHR⁵;

with the proviso that when E is -SO- or -SO₂-, D is not -NH-CHR²-, or -O=CHR²;

R¹ is hydrogen, halogen, or C₁-C₆ alky1;

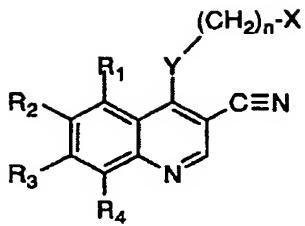
R², R³, and R⁴ are independently hydrogen, C₁-C₆ alky1,-(CH₂)_n-N-piperidiny1, -(CH₂)_n-N-piperaziny1,

-(CH₂)_n-N₁-piperaziny1 [N₄-(C₁-C₆)alky1],

$-(CH_2)_n$ -N-pyrrolidyl, $-(CH_2)_n$ -N-pyridinyl,
 $-(CH_2)_n$ -N-imidazoyl, $-(CH_2)_n$ -imidazoyl
 $-(CH_2)_n$ -N-morpholino,
 $-(CH_2)_n$ -N-thiomorpholino,
 $-(CH_2)_n$ -N-hexahydroazepine or substituted C₁-C₆ alkyl,

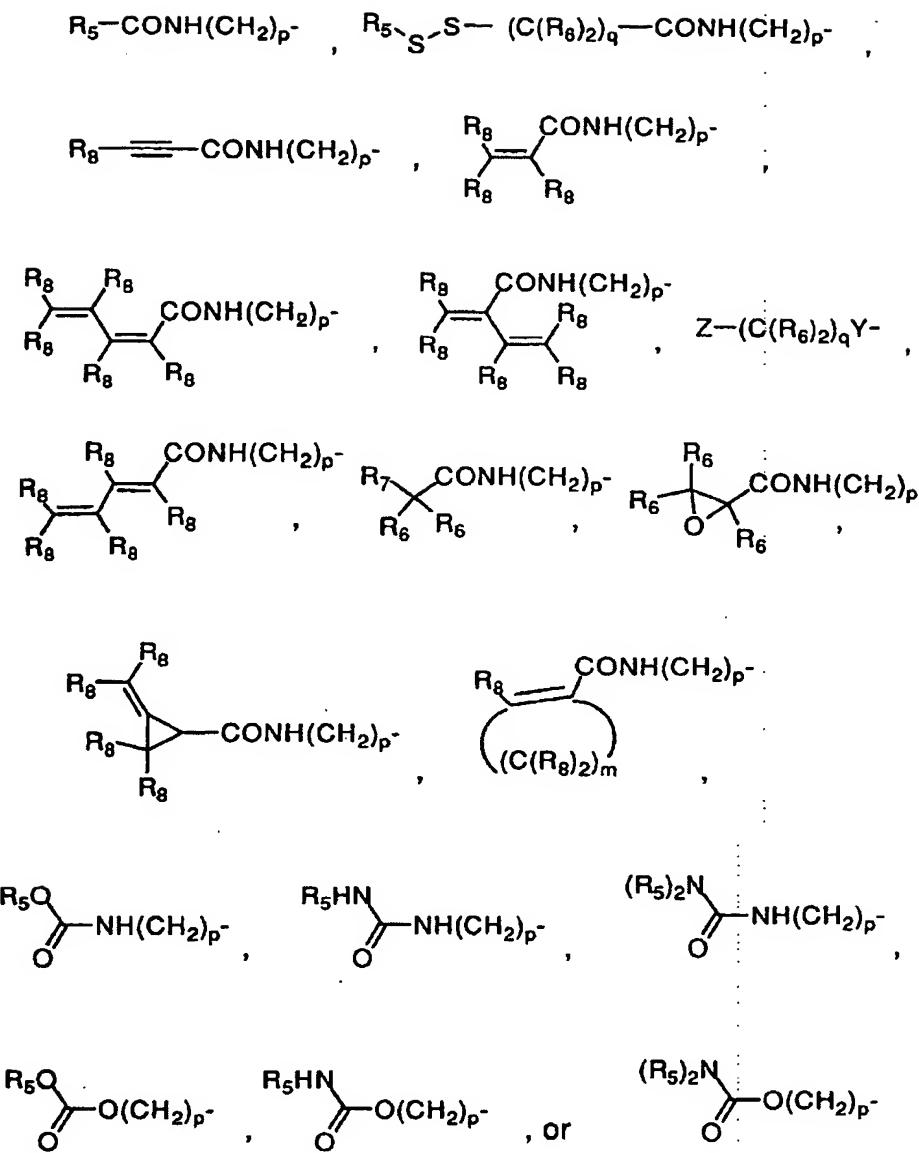
wherein the substituents are selected from -OH, -NH₂, or -NA-B, A and B are independently hydrogen, C₁-C₆ alkyl, -(CH₂)_nOH, -(CH₂)_n-N-piperidinyl, -(CH₂)_n-N-piperazinyl, -(CH₂)_n-N₁-piperazinyl[N₄-(C₁-C₆ alkyl)], -(CH₂)_n-N-pyrrolidyl, -(CH₂)_n-N-pyridyl, -(CH₂)_n-imidazoyl or -(CH₂)_n-N-imidazoyl; Z¹, Z², or Z³ are independently hydrogen, halogen, C₁-C₆ alkyl, C₃-C₈ cycloalkyl, C₁-C₆ alkoxy, C₃-C₈ cycloalkoxy, nitro, C₁-C₆ perfluoroalkyl, hydroxy, C₁-C₆ acyloxy, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, -NH(C₃-C₈ cycloalkyl), -N(C₃-C₈ cycloalkyl)₂, hydroxymethyl, C₁-C₆ acyl, cyano, azido, C₁-C₆ thioalkyl, C₁-C₆ sulfinylalkyl, C₁-C₆ sulfonylalkyl, C₃-C₈ thiocycloalkyl, C₃-C₈ sulfinylcycloalkyl, C₃-C₈ sulfonylcycloalkyl, mercapto, C₁-C₆ alkoxycarbonyl, C₃-C₈ cycloalkoxycarbonyl, C₂-C₄ alkenyl, C₄-C₈ cycloalkenyl, or C₂-C₄ alkynyl; and R⁵ is hydrogen, halogen, C₁-C₆-perfluoroalkyl, 1,1-difluoro(C₁-C₆)alkyl, C₁-C₆alkyl, -(CH₂)_n-N-piperidinyl, -(CH₂)_n-piperazinyl, -(CH₂)_n-piperazinyl[N₄-(C₁-C₆)alkyl], -(CH₂)_n-N-pyrrolidyl, -(CH₂)_n-pyridinyl, -(CH₂)_n-imidazoyl, -(CH₂)_n-N-morpholino, -(CH₂)_n-N-thiomorpholino, -CH=CH₂, -CH=CH-(C₁-C₆), N-hexahydroazepine, -(CH₂)_nNH₂, -(CH₂)_nNH(C₁-C₆ alkyl), -(CH₂)_n-N(C₁-C₆ alkyl)₂, -1-oxo(C₁-C₆)alkyl, carboxy, (C₁-C₆)alkyloxycarbonyl, N-(C₁-C₆)alkylcarbamoyl, phenyl or substituted phenyl, wherein the substituted phenyl may have from one to three substituents independently selected from Z¹, Z², Z³ or a monocyclic heteroaryl group, and each C₁-C₆ alkyl group may be substituted with -OH, -NH₂ or -NAB, (wherein A and B are as defined above), R⁶ is hydrogen or C₁-C₆ alkyl; and n is 1 to 4, p is 0 or 1.

11. (Currently Amended) The preventive and/or therapeutic agent according to claim 1 or claim 3 or claim 5 containing a compound having inhibitory activity to epidermal growth factor receptor represented by the chemical formula VI, a stereoisomer thereof, a pharmaceutically-acceptable salt thereof, its hydrate or its solvate as the effective ingredient,



<Formula VI>

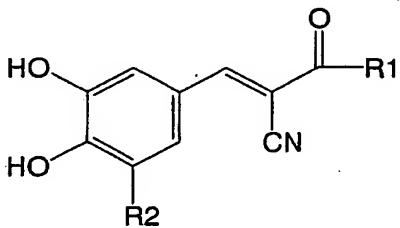
wherein X is cycloalkyl of 3 to 7 carbon atoms, which may be optionally substituted with one or more alkyl groups having 1 to 6 carbon atom; or is a pyridinyl, pyrimidinyl, or phenyl ring; wherein the pyridinyl, pyrimidinyl, or phenyl ring may be optionally mono-, di-, or tri-substituted with a substituent selected from the group consisting of halogen, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, azido, hydroxyalkyl of 1-6 carbon atoms, halomethyl, alkoxymethyl of 2-7 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkoxy of 1-6 carbon atoms, alkylthio of 1-6 carbon atoms, hydroxy, trifluoromethyl, cyano, nitro, carboxy, carboalkoxy of 2-7 carbon atoms, carboalkyl of 2-7 carbon atoms, phenoxy, phenyl, thiophenoxy, benzoyl, benzyl, amino, alkylamino of 1-6 carbon atoms, dialkylamino of 2 to 12 carbon atoms, phenylamino, benzylamino, alkanoylamino of 1-6 carbon atoms, alkenoylamino of 3-8 carbon atoms, alkynoylamino of 3-8 carbon atoms, and benzoylamino; n is 0-1; Y is -NH-, -O-, -S-, or -NR-; R is alkyl of 1-6 carbon atoms; R₁, R₂, R₃, and R₄ are each independently, hydrogen, halogen, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, alkenyloxy of 2-6 carbon atoms, alkynyoxy of 2-6 carbon atoms, hydroxymethyl, halomethyl, alkanoyloxy of 1-6 carbon atoms, alkenoyloxy of 3-8 carbon atoms, alkynoyloxy of 3-8 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkenoyloxymethyl of 4-9 carbon atoms, alkynoyloxymethyl of 4-9 carbon atoms, alkoxymethyl of 2-7 carbon atoms, alkoxy of 1-6 carbon atoms, alkylthio of 1-6 carbon atoms, alkylsulphinyl of 1-6 carbon atoms, alkylsulphonyl of 1-6 carbon atoms, alkylsulfonamido of 1-6 carbon atoms, alkenylsulfonamido of 2-6 carbon atoms, alkynylsulfonamido of 2-6 carbon atoms, hydroxy, trifluoromethyl, cyano, nitro, carboxy, carboalkoxy of 2-7 carbon atoms, carboalkyl of 2-7 carbon atoms, phenoxy, phenyl, thiophenoxy, benzyl, amino, hydroxyamino, alkoxyamino of 1-4 carbon atoms, alkylamino of 1-6 carbon atoms, dialkylamino of 2 to 12 carbon atoms, aminoalkyl of 1-4 carbon atoms, N-alkylaminoalkyl of 2-7 carbon atoms, N,N-dialkylaminoalkyl of 3-14 carbon atoms, phenylamino, benzylamino,



wherein, R_5 is alkyl of 1-6 carbon atoms, alkyl optionally substituted with one or more halogen atoms; phenyl, or phenyl optionally substituted with one or more halogen, alkoxy of 1-6 carbon atoms, trifluoromethyl, amino, nitro, cyano, or alkyl of 1-6 carbon atoms groups; R_6 is hydrogen, alkyl of 1-6 carbon atoms, or alkenyl of 2-6 carbon atoms; R_7 is chloro or bromo; R_8 is hydrogen, alkyl of 1-6 carbon atoms, aminoalkyl of 1-6 carbon atoms, N-alkylaminoalkyl of 2-9 carbon atoms, N,N-dialkylaminoalkyl of 3-12 carbon atoms, N-cycloalkylaminoalkyl of 4-12 carbon atoms, N-cycloalkyl-N-alkylaminoalkyl of 5-18 carbon atoms, N,N-dicycloalkylaminoalkyl of 7-18 carbon atoms, morpholino-N-alkyl

(wherein the alkyl group has 1-6 carbon atoms), piperidino-N-alkyl (wherein the alkyl group has 1-6 carbon atoms), N-alkyl-piperidino-N-alkyl (wherein either alkyl group has 1-6 carbon atoms), azacycloalkyl-N-alkyl of 3-11 carbon atoms, hydroxyalkyl of 1-6 carbon atoms, alkoxyalkyl of 2-8 carbon atoms, carboxy, carboalkoxy of 1-6 carbon atoms, phenyl, carboalkyl of 2-7 carbon atoms, chloro, fluoro, or bromo; Z is amino, hydroxy, alkoxy of 1-6 carbon atoms, alkylamino (wherein the alkyl moiety has 1-6 carbon atoms), dialkylamino (wherein each of the alkyl moieties has 1-6 carbon atoms), morpholino, piperazino, N-alkylpiperazino (wherein the alkyl moiety has 1-6 carbon atoms), or pyrrolidino; m = 1-4, q = 1-3, and p = 0-3; any of the substituents R₁, R₂, R₃, or R₄ that are located on contiguous carbon atoms may together be the divalent group -O-C(R₈)₂-O- (with the proviso that when Y is -NH-, R₁, R₂, R₃, and R₄ are hydrogen, and when n is 0, X is not 2-methylphenyl).

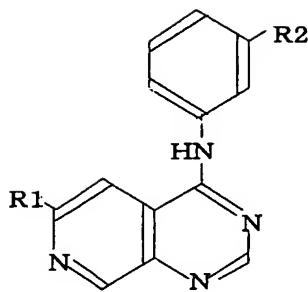
12. (Currently Amended) The preventive and/or therapeutic agent according to claim 1-~~or claim 3 or claim 5~~ containing a cinnamide derivative represented by the chemical formula VII, a stereoisomer thereof, a pharmaceutically-acceptable salt thereof, its hydrate or its solvate as the effective ingredient,



<Formula VII>

wherein R1 is preferably hydroxy, amino, alkylamino or phenyl amino group and R2 is preferably hydrogen, hydroxyl, nitro or t-butyl group.

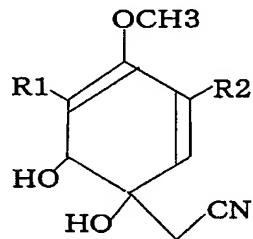
13. (Currently Amended) The preventive and/or therapeutic agent according to claim 1-~~or claim 3 or claim 5~~ containing a pyridopyrimidine derivative represented by the chemical formula VIII, a stereoisomer thereof, a pharmaceutically-acceptable salt thereof, its hydrate or its solvate as the effective ingredient,



<Formula VIII>

wherein R1 is preferably hydroxyl, amino, lower alkylamino, amide, alkylamide, alkenesulfinyl, or alkeneoxyamino group and R2 is preferably hydrogen or acetylene group.

14. (Currently Amended) The preventive and/or therapeutic agent according to claim 1 or claim 3 or claim 5 containing a tyrosine derivative represented by the chemical formula IX, a stereoisomer thereof, a pharmaceutically-acceptable salt thereof, its hydrate or its solvate as the effective ingredient,



<Formula IX>

wherein R1 and R2 are preferably halogen atoms.

15. (Currently Amended) The preventive and/or therapeutic agent according to claim 1 (1) or (3) or (5) containing 4-(3-chloro-4-fluoroanilino)-7-methoxy-6-(3-morpholinopropoxy)quinazoline, a stereoisomer thereof, a pharmaceutically-acceptable salt thereof, its hydrate or its solvate as the effective ingredient.

16. (Currently Amended) The preventive and/or therapeutic agent according to claim 1 (1) or (3) or (5) containing {4-(3-bromophenyl)anilino}-6,7-diamino quinazoline, a stereoisomer thereof, a pharmaceutically-acceptable salt thereof, its hydrate or its solvate as the effective ingredient.